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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,722	10/23/2003	Jerome B. Zeldis	9516-078-999	2389

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EXAMINER	
OLSON, ERIC	
ART UNIT	PAPER NUMBER
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,722	ZELDIS ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9,23 and 27-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 9, 23, and 27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted March 12, 2007 wherein claims 1, 2, 23, and 27 are amended, claims 6 and 8 are cancelled, and new claims 28-34 are introduced. This application claims priority to provisional application 60/421004, filed October 24, 2002.

Claims 1-5, 9, 23, and 27-34 are pending in this application.

Claims 1-5, 9, 23, and 27-34 as amended are examined on the merits herein.

Applicant's amendment, submitted March 12, 2007, with respect to the objection to claim 27 for being in improper multiple dependant form, has been fully considered and found to be persuasive to remove the objection as the claim as amended depends from only one base claim. Therefore the objection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 1-6, 8-9, 23, and 27 under 35 USC 112, first paragraph, for lacking enablement for a method of preventing or modifying pain, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn solely to a method of treating a disorder. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 1-6, 8-9, and 23 under 35 USC 112, first paragraph, for lacking enablement for a method involving any cytokine inhibitory drug whatsoever, has been

fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method involving a specific drug. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 1, 6, 8, and 9 under 35 USC 102(b), for being anticipated by Rajkumar et al., has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method involving a specific drug that is not thalidomide. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 1 and 6 under 35 USC 102(e), for being anticipated by Olmarker et al., has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method of treating complex regional pain syndrome, which is not a nerve root injury. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 1, 6, 8, and 9 under 35 USC 103, for being obvious over Rajkumar et al. in view of Merck, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method involving a specific drug that is not thalidomide. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claim 27 under 35 USC 103, for being obvious over Olmarker et al. in view of Muller et al., has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method of treating complex regional pain syndrome, which is not a nerve root injury. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 2-5 and 23 under 35 USC 103, for being obvious over Olmarker et al. in view of Merck, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method of treating complex regional pain syndrome, which is not a nerve root injury. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 1, 6, and 27 under the doctrine of obviousness-type double patenting, for claiming the same invention as any of US patents 6020358, 6011050, or 6635250, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method of treating complex regional pain syndrome, which is not a nerve root injury. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 1 and 6 under the doctrine of obviousness-type double patenting, for claiming the same invention as any of US patents 5635517, 5955476, 5798368, 5698579, 5736570, 5703098, 6395754, 6180644, 6130226, 6075041, 6214857, or 5968945, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method of treating complex regional pain syndrome, which is not a nerve root injury, and do not recite the specific chemical compound claimed by the instant claims. Therefore the rejection is withdrawn.

The following new grounds of rejection are introduced:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

> applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 9, and 27-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Schafer et al. (PCT international publication WO03080049, reference included with PTO-1449 July 26, 2004) Schafer et al. discloses a method of treating various diseases by administering the compound (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione, which is the compound of the claimed invention. (p. 4, lines 1-4, p. 6, lines 1-5) One of the diseases that can be treated in his manner is complex regional pain syndrome. (p. 11, lines 9-15) The compounds can be administered with an additional therapeutic agent as well. (p. 13, lines 8-9) The compound can be administered as a pharmaceutically acceptable salt or solvate, (p. 18, lines 34-35) by oral administration as tablets or capsules, (p. 19, lines 9-20) in a daily dosage of 10-200 mg per day. (p. 21, lines 3-15) Thus the claimed invention is anticipated by Schafer et al.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-5 and 23 are rejected under 35 U.S.C. 103(a) as being obvious over Schaffer et al. (PCT international publication WO03080049, reference included with PTO-1449 July 26, 2004) in view of the Merck manual of diagnosis and therapy, seventeenth edition. (Herein referred to as Merck, reference of record in previous office action) Schaffer et al. does not disclose a method further comprising administering the additional therapeutic agents of instant claims 3-5 or the therapies of instant claim 23.

Merck discloses that complex regional pain syndrome may be treated with several drugs including nifedipine, prednisone, opioid analgesics, tricyclic antidepressants, and anticonvulsants. (p. 1373, left column, second paragraph) It should be noted that it is well known in the art that opioid analgesics include oxycodone, tricyclic antidepressants include amitryptyline, imipramine, and doxepin, and anticonvulsants include gabapentin. Merck also discloses that physical therapy is essential throughout therapy for complex regional pain syndrome (p. 1373, left column, last paragraph) and that pain relief that outlasts the administration of a sympathetic block but is still transitory suggests the need for surgery. (p. 1373, left column, second paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of Schaffer et al. for the treatment of complex regional pain syndrome further comprising administering one or more of the pharmaceutical active agents described by Merck and still further administering physical therapy and/or surgery. One of ordinary skill in the art would have been motivated to combine these teachings because Schaffer et al. and Merck both disclose their respective teaching as being useful for treating the same condition, namely complex regional pain syndrome. One of ordinary skill in the art would reasonably have expected success because combining two treatments known in the prior art to be effective for treating the same disorder by different methods is reasonably expected to produce at least additive effects.

Thus the invention taken as a whole is *prima facie* obvious.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the

application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 1, 9, and 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omoigui (US patent publication 20040038874, cited in PTO-1449 July 26, 2004) in view of Muller et al. (US patent 6020358, cited in PTO-1449 July 26, 2004) Omoigui discloses a method for the treatment of persistent pain by administering a drug that antagonizes one or more mediators of inflammation. (p. 1, paragraph 0004) Drugs useful in this manner include TNF-α blockers. (p. 2, paragraphs 0007 and 0011) Reflex Sympathetic Dystrophy, otherwise known as chronic regional pain syndrome, is listed as a disease treatable by this method. (pp. 9-10, paragraphs 0078-0082) Omoigui does not disclose a therapeutic method comprising administering the specific TNF-α inhibitor (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione, or one involving a pharmaceutical dosage form having the specific limitations of instant claims 28-34.

Muller et al. discloses that compounds of a general formula including that of the claimed compound (column 5, line 1) are capable of decreasing the levels of TNF-α in a patient, (column 4, lines 55-67) thus qualifying as a TNF-α blocker. Example 12 (column 14, lines 35-55) is the exact same compound (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione disclosed in

the instant claims. Muller et al. also discloses oral dosage forms of this compound as tablets or capsules, having a unit dosage of 1-100 mg, along with another dosage form in isotonic saline, a pharmaceutically acceptable solvate. (column 9, lines 22-52)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the compound of example 12 of Muller et al. in the method of Omoigui, in an appropriate dosage form as disclosed by Muller et al. One of ordinary skill in the art would have been motivated to use this compound and dosage form because it is disclosed by Muller et al. to be useful for lowering TNF-α levels in a subject. One of ordinary skill in the art would reasonably have expected success because the scope of Omoigui includes all compounds capable of inhibiting or otherwise blocking the activity of TNF-α.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 2-5 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omoigui (US patent publication 20040038874, cited in PTO-1449 July 26, 2004) in view of Muller et al. (US patent 6020358, cited in PTO-1449 July 26, 2004) as applied to claims 1, 9, and 27-34 above, and further in view of Merck. (Reference of record in previous office action) The disclosure of Omoigui in view of Muller et al. is discussed above. Omoigui in view of Muller et al. does not disclose a method further comprising administering the additional therapeutic agents of instant claims 2-5 or the therapies of instant claim 23.

Merck discloses that complex regional pain syndrome may be treated with several drugs including nifedipine, prednisone, opioid analgesics, tricyclic antidepressants, and anticonvulsants. (p. 1373, left column, second paragraph) It should be noted that it is well known in the art that opioid analgesics include oxycodone, tricyclic antidepressants include amitryptyline, imipramine, and doxepin, and anticonvulsants include gabapentin. Merck also discloses that physical therapy is essential throughout therapy for complex regional pain syndrome (p. 1373, left column, last paragraph) and that pain relief that outlasts the administration of a sympathetic block but is still transitory suggests the need for surgery. (p. 1373, left column, second paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of Omoigui et al. for the treatment of complex regional pain syndrome further comprising administering one or more of the pharmaceutical active agents described by Merck and still further administering physical therapy and/or surgery. One of ordinary skill in the art would have been motivated to combine these teachings because Omoigui et al. and Merck both disclose their respective teaching as being useful for treating the same condition, namely complex regional pain syndrome. One of ordinary skill in the art would reasonably have expected success because combining two treatments known in the prior art to be effective for treating the same disorder by different methods is reasonably expected to produce at least additive effects.

Thus the invention taken as a whole is *prima facie* obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over either claims 1, 6, 12, and 17 of U.S. Patent No. 6020358 (Reference cited in PTO-1449 July 26, 2004, herein referred to as '358) or alternately claims 1, 4, 10, and 15 of U.S. Patent No. 6011050 (Reference cited in PTO-1449 July 26, 2004, herein referred to as '050) in view of Omoigui. (US patent publication 20040038874, cited in PTO-1449 July 26, 2004 July 26, 2004) Claim 17 of '358 and claim 15 of '050 are both drawn to methods of reducing undesirable levels of TNF-α in a mammal by administering a compound having a generic structure which includes within its breadth the species recited in instant claim 27. Claims 6 and 12 of

'358 and 4 and 10 of '050 further suggest the claimed structure by defining R4, R5, and R6. Said claims do not disclose a method of treating neuropathic pain in this manner.

Omoigui discloses a method for the treatment of persistent pain by administering a drug that antagonizes one or more mediators of inflammation. (p. 1, paragraph 0004) Drugs useful in this manner include TNF-α blockers. (p. 2, paragraphs 0007 and 0011) Reflex Sympathetic Dystrophy, otherwise known as chronic regional pain syndrome, is listed as a disease treatable by this method. (pp. 9-10, paragraphs 0078-0082)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the methods of Claim 17 of '358 and claim 15 of '050 on a mammal suffering from neuropathic pain caused by a herniated disk. One of ordinary skill in the art would have been motivated to practice the invention in this manner because claims 1, 21, and 27 of '250 disclose that blocking the action of TNF-α is an effective strategy for treating neuropathic pain in a herniated disk. One of ordinary skill in the art would have reasonably expected success because claims 1, 21, and 27 of '250 already demonstrate the utility of this method.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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